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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
GOLLAMUDI, SHARMILA S	

ART UNIT	PAPER NUMBER
1616	

DATE MAILED: 07/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/745,095	APPEL ET AL.	
	Examiner	Art Unit	
	Sharmila S. Gollamudi	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 May 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2, 7-9, 12-32, 44-45, 49-51, 56-57, 63-81, 88-97, 101, 103-108, 118-122, 124, 130-131* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims pending in the application are 2,7-9,12-32,44,45,49-51,56,57,63-81,88-97,101,103-108,118-122,124,130 and 131.

DETAILED ACTION

Receipt of Amendments/Remarks received on May 3, 2004 is acknowledged. Supplemental Response, Remarks, and Information Disclosure Statement received on May 5, 2004 is acknowledged. Claims **2, 7-9, 12-32, 44-45, 49-51, 56-57, 63-81, 88-97, 101, 103-108, 118-122, 124, 130-131** are pending in this application.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on May 5, 2004 has been considered by the examiner and an initialed copy of PTO-1449 has been attached to the following Office Action.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 45 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 45 recites wherein the swelling agent is selected from sodium starch glycolate and sodium croscarmellose, however claim 45 depends on independent claim 2 which requires the swelling agent is selected from sodium starch glycolate and sodium croscarmellose. Therefore, it is unclear what the intended limitation of claim 45 is.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 2, 7-9, 12-32, 44-45, 49-51, 56, 63-81, 88-97,101, 103-108, 118-122, 124, and 130-131 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wong et al (4,765,989) in view of Stevens et al (5,897,874), optionally in further view of Park et al (6,271,278).

Wong et al teach an osmotic device for administering drugs in various shapes and forms. The object of the device is to provide a therapeutic device that administers a complete pharmaceutical regimen at a controlled and continuous time period. The device also provides dispending to the gastric tract at a controlled rate. See column 3. The device contains a first composition containing a drug, polyethyleneoxide (PEO) (drug entertaining agent), hydroxypropylmethylcellulose (HPMC) (concentration enhancing polymer), and magnesium stearate. The second expanding composition contains PEO (swelling agent), instant HPMC tabletting aid), sodium chloride, and magnesium stearate. See examples, especially 3. The osmopolymers are swellable and hydrophilic polymers, which swell and expand in aqueous medium. See column 15, lines 61-68. The osmopolymers used in the invention have an

expansion and are utilized in both the firstly layer and second layer, which may be different or the same (col. 16, lines 3-5). The osmopolymers utilized may be a variety of hydrophilic polymers such as PEO polymers or a mixture of methylcellulose, crosslinked agar and carboxymethyl cellulose. See column 16, lines 20-23 and line 36. The mass ratio of the first composition to the second composition is taught on column 16. The general concept of swelling ratio is taught on columns 17 and 18. Wong teaches the active agent may in various forms and dispersed in suspending agents such as PVP (col. 18, line 43 to col.19, line 5). Agents such as tartaric acid (solubilizers), mannitol (fluidizers), sucrose, and sodium chloride are taught. The reference teaches a semipermeable wall that allows water to enter the core. A semipermeable wall made of 95% cellulose acetate having an acetyl content of 39.8% and 5% PEG surrounds the two compositions. The coating has pore sizes of 10 angstorm to 100 microns See column 10 to column 11, line 20. . Solvents for the semipermeable membrane are taught on column 20, lines 11-35. Release of the drug is taught in Figure 9. Wong teaches several shapes such as in Figure 5, wherein rather than have one port as seen in a tablet, the device as several pores to allow the passage of water. Wong teaches that the shape of the tablet and capsule shape are different, but they act in a similar manner to let fluid into the core. See column 8-9. Solvents for the semipermeable membrane are taught on column 20, lines 11-35. Release of the drug is taught in Figure 9.

Wong does not teach instant parameters (the instant swelling ratio and core strength) and swelling agents or instant amount of tabletting aids.

Stevens et al teach a delivery device with a drug and expandable excipient. The dosage form may be in tablet form. See abstract and examples. The device has an impermeable coating

formed from a water-soluble material, which is preferably but not limited to capsules wherein the capsule contains the expandable excipient. See column 3, lines 13-21. The expandable excipients may also be used in a solid pharmaceutical dosage forms such as compressed powders (tablets) or cast forms. See column 4, lines 1-6. The expandable excipient is made of a solid material whose volume increases due to the absorption of water from the surrounding medium and has a water-swellable material that has the overall swelling capacity of 200-400% (col. 4, lines 44-48). The swellable materials may be chosen from water-swellable hydrogel polymers: PEO polymers with a molecular weight of 4,000-12,000 or known pharmaceutical disintegrants, i.e. sodium starch glycolate, microcrystalline cellulose, etc., which swell rapidly and completely after administration, thereby disrupting or breaking up the solid dosage form. See column 4, lines 10-30. The expandable excipients also contain wetting agents (sodium lauryl sulfate) up to 2%, lubricants such as magnesium stearate and silica up to 1%, and water-soluble sugars up to 10%. Stevens teaches the conventional hardness of a tablet is 4kg and the instant tablet may have the strength of conventional tablets or less, i.e. 2kg (col. 5, lines 5-70). The drug may be mixed with a carrier material and is positioned over the hydrogel layer (col. 6, lines 26-27). The swelling factor is taught on column 7. The device has the advantage of containing expandable excipients that are designed to improve the expulsion of the active in a particular region such as the gastric tract that has low water content. See column 5. Example 10 discloses a disintegrant tablet containing 24% low-substituted cellulose (L-HPC), 24% Avicel (microcrystalline cellulose), and 50% EXPLOTAB (sodium starch glycolate). This combination of Avicel and EXPLOTAB provide for instant swelling ratio.

Park et al teach a hydrogel composition having fast swelling and high mechanical strength. The superporous hydrogel composite is formed by polymerizing one or more ethylenically-unsaturated monomers, and a crosslinking agent, in the presence of particles of a disintegrant. The disintegrant such as crosslinked sodium carboxymethylcellulose, crosslinked sodium starch glycolate, and crosslinked PVP, rapidly absorbs water and serves to increase mechanical strength. See abstract. Park discloses that the limiting factor of hydrogels have been their slow swelling property which usually takes several hours and this it too slow for many applications when fast swelling is essential. Park discloses that although hydrogels have been successfully used as gastric retention devices that stay in the stomach for several hours, the hydrogels had to be preswollen before administering to avoid premature emptying into the intestine. Further, Park discloses to increase swelling properties, the mechanical strength decreases; however by adding the disintegrant, the mechanical strength is increased. See column 4, lines 10-45 and column 26. Swelling ratios are taught on Table 2. Compression is taught in Figure 4A in kg/cm2. Park teaches that in the controlled drug delivery area superporous hydrogel and superporous hydrogel composites can be used as a platform for long-term oral drug delivery.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Wong et al and Steven et al and utilize the instant swelling agent. One would be motivated to utilize the instant swelling agent in the expandable hydrogel portion of Wong's since Stevens et al discloses the advantages of the instant swelling agent, which provides the instant swelling ratio. The swelling capacity of the instant agents improve the release of an active in the gastro-intestinal tract, i.e. to provide for the complete release of the active from the body. Therefore, the selection of conventional polymers and disintegrants

utilized in the art for the same purpose, which are characterized by a specific swelling capacity, to yield a certain swelling ratio is deemed obvious since the swelling capacity/ratio determines the rate of release of the active agent from the device, i.e. the "push" of the active out of the body. Thus, it is prima facie obvious to manipulate the selection of the swelling agent(s) and amount to yield a desired release rate. Lastly, one would expect similar results since Wong's expandable portion contains PEO polymers and Stevens teaches that the hydrogel may be PEO polymer or in an alternative embodiment the PEO polymers may be substituted with the instant swelling agent to enhance to rate of deliver since the swelling agent rapidly absorbs water or optionally mixing of swelling agents.

Additionally, it would have been obvious to one of ordinary skill in the art at the time the invention was made to further look at Park et al and utilize instant swelling agents Park discloses that a fast swelling hydrogel and superswelling is important for controlled oral dosage forms, however prior art hydrogels have decreased mechanical strength as the swelling capacity is increased. Thus, Park states that instant swelling agents are improvement since they not only possess super swelling capacity but also provide increased mechanical strength to hydrogels. Therefore, one would be motivated to add the instant swelling agent since it not only increases the swelling capacity of the hydrogel but it increases the mechanical strength. Furthermore, Park's teaching support the examiner's position that Stevens's expandable excipient implicitly has the instant strength.

Response to Arguments

Applicant argues that the amended claims now require 20% of a tabletting aid selected from a Markush group that does not include Wong's magnesium stearate. Applicant argues that

Stevens in contrast to the amended claims, does not teach the instant amount of tabletting aid and teaches smaller amounts of the tabletting aid. Applicant argues that neither reference teaches a high swelling ratio combined with high strength. Applicant states that the Rule 132 declaration provides evidence that Wong does not teach the instant swelling ratio and that a combination of PEO and sodium chloride does not provide such a ratio. Lastly, applicant argues that Stevens is concerned with a capsule and claims have been amended to recite that the dosage form is a tablet, thus one would not look to Stevens.

Applicant's arguments filed have been fully considered but they are not persuasive. Firstly, the examiner again points out that the Rule 132 declaration submitted on January 2003 was relevant solely for the purpose of establishing the prior art did not anticipate the instant invention and did not inherently have said parameters. Further, the Rule 132 declaration was based on US patent 5,620,705 to Dong. The instant rejection is based on US patent 4,765,989 to Wong et al. More specifically, the examiner reiterates that the applicant has not provided a Rule 132 based on US 4,765,989 wherein Wong utilizes PEO polymer and instant tabletting aid HPMC in the water-swellable composition. Therefore, discussions of the Rule 132 declaration are irrelevant to the instant rejection.

The examiner recognizes the deficiency in Wong et al, namely the instant amount of amended tabletting aid and instant swelling agents as currently recited. Thus, the examiner relies on Stevens to cure the deficiency. Stevens teaches the instant swelling agents and instant swelling agent and tabletting aid combination in instant amounts. Applicant is incorrect in his statement that Stevens teaches a minor amount of the expandable excipient. Applicant has construed the cited passage incorrectly. Stevens states in the cited passage that the expandable

excipient may contains minor adjuncts such as wetting agents, sugars, wicking agents, etc. up to 10%. However, this "minor" amount is not in reference to the expandable excipient. The examples aptly demonstrate this. Note example 10 wherein Avicel (microcrystalline cellulose), i.e. applicant's tabletting aid, is utilized in the amount of 24% in combination with 50% Explotab, i.e. applicant's swelling agent, and 24% of HPC. Thus, clearly Stevens teaches the same combination in the same concentration range to yield the instant swelling ratio.

Stevens states that the swelling capacity (note that swelling capacity and swelling ratio are related) of each polymer defines the rate of release since the hydrogel pushes the active out of the device. The instant swelling agent provides for certain advantages such as rapid swelling which completely pushes the active out of the device. Thus, the motivation to use the instant swelling ratio, which is provided by Stevens' teaching, is to manipulate the release rate of the active agent. Wong teaches that the osmopolymer (swelling agent) may be a variety of materials that are hydrophilic and capable of absorbing water. Wong exemplifies the use of a high molecular weight PEO with HPMC. Stevens also teaches the use of high molecular weigh PEO polymers or as an alternative the hydrophilic polymers may be replaced with conventional disintegrants such as instant starch glycolate (Explotab) and microcrystalline cellulose which enhance delivery of the active. Therefore, the motivation to look to Stevens is an enhanced delivery of an active agent.

In regards to the unexpectedness of the tablet strength and swelling ratio, the examiner points out that the applicant has not provided any evidence to substantiate unobviousness. Further, it is the examiner's position that Stevens teaches the instant parameters and manipulation of the parameters is a skill within the art.

Lastly in regards to the argument that Stevens only teaches capsules, the examiner points out that the secondary reference is solely relied upon for the swelling material and the swelling ratio; Wong encompasses the broad aspect of the invention of the tablet. Firstly, the examiner points out that Wong teaches that the device may be in a capsule or tablet form since both act in a similar manner of pushing the agent out of the device. The examiner notes that Stevens teaches a end product of a capsule, however the hydrogel is in a tablet form and since Stevens' capsule also functions in a similar manner wherein the active layer is pushed out by the hydrogel layer, it is reasonable for skilled artisan to ascertain that Stevens' expandable excipients may also be used in a tablet device.

Claim 57 under 35 U.S.C. 103(a) as being unpatentable over Wong et al (4,765,989) in view of Stevens et al (5,897,874), optionally in further view of Park et al (6,271,278), in further view of From hypertension to angina to Viagra (Jim Kling, Modern Drug Discovery, 1998, 1(2), pg.31, 33-34, 36, 38) is maintained.

As set forth above, Wong and Stevens teach delivery devices containing expandable excipients. Wong teaches the suitability of several drugs such as antihypertensives.

Wong and Stevens do not teach instant drug

Kling teaches Viagra as a drug for hypertension or erectile dysfunction.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use sildenafil citrate in the device of Wong or Stevens. One would be motivated to do so if one wanted to treat erectile dysfunction and it is obvious for an artisan to choose the drug depending on the symptoms and disease to be treated. Further, one would be motivated to

do so with the expectation of similar results since Wong teaches the use of antihypertensives in the device.

Response to Arguments

Applicant argues that King does not cure the fatal flaws of Wong et al and Stevens et al.

Applicant's arguments filed have been fully considered but they are not persuasive. The merits of Wong et al and Stevens et al have been discussed above. The examiner merely relies on King to teach the instant active agent. The choice of the active agent depends on the symptoms to be treated. Therefore, if one were motivated to treat erectile dysfunction and hypertension, then one would utilize the instant active agent.

Conclusion

No claims are allowed at this time.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharmila S. Gollamudi whose telephone number is 571-272-0614. The examiner can normally be reached on M-F (8:00-5:30), alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on 571-272-0887. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Sharmila S. Gollamudi
Examiner
Art Unit 1616

SSG

MICHAEL G. HARTLEY
PRIMARY EXAMINER